REMARKS

Applicants have amended claim 1 to more clearly define the invention. This amendment is supported at page 6, paragraphs 1-3, as well as Figures 2-3. This amendment does not introduce new matter, and its entry is respectfully requested. Claims 2 and 4 have been rewritten as independent claims. Claim 2 has been amended to make explicit that which was implicit, namely that the gradient array has at least two rows of microchannels. This amendment is supported at page 6, paragraph 3. Claim 2 has also been amended to make explicit that which was implicit, namely that each microchannel has an entry portion and an exit portion. This amendment is supported by page 8, paragraph 2, and Figure 3b. The amendment to claim 3, indicating that the channel is wedge-shaped, is supported by page 9, paragraph 2. Claim 4 has been amended to indicate that the array has a plurality of microchannels for capturing a cell; this amendment is supported at page 8, paragraph 2. As such, these amendments do not introduce new matter, and their entry is respectfully requested.

Claims 1 – 18 were rejected under 35 U.S.C. § 112, second paragraph.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

To expedite prosecution, applicants have amended claim 1 to correct a clerical error and to recite that each microchannel has an entry portion and an exit portion, rather than an exit "channel." Applicants respectfully submit that this amendment has obviated the rejection, and respectfully request its withdrawal.

Claims 1- 18 were rejected under 35 U.S.C. § 102(b) as being anticipated by Sutton et al.

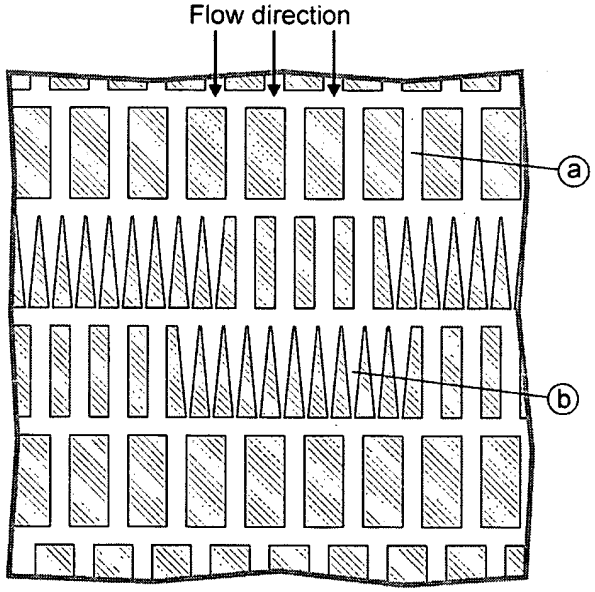
Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The present invention is directed to a human erythrocyte microchannel analyzer, or HEMA, which enables morphological measurements of a large number of individual cells to be rapidly determined. The claims define a structure that traps or captures cells. Previous technologies allowed measurements of either a *population* of red blood cells, but not the

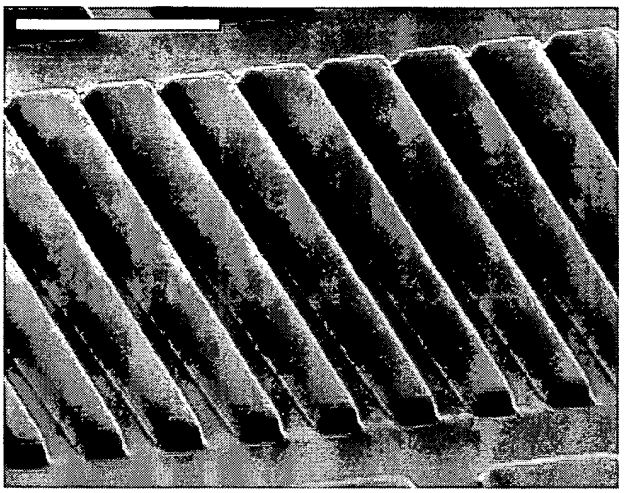
properties of individual cells within the population, or measurements of *individual* cells, which could not be collected in large numbers. In the instant instrument, the cells are trapped for analysis in microfabricated channels. In several preferred embodiments, the HEMA uses the position of the cell after it has come to rest in a specific location; in other words, it takes a static measurement. This trapping is accomplished by having a structure where the cells enter a wedge-shaped structure that is wider at the entrance or has at least a first and second set of microchannels with the first set having a cross-sectional area larger than said second cross-sectional area.

The structure of the present instrument is fundamental to its function, and is entirely different from instruments in the prior art, including that of Sutton. Applicants have previously submitted a publication of the applicants which describes in great detail the structure and function of the claimed instrument. (Gifford et al., Biophys. J. 84: 623-633 (2003).) Applicants are reprinting here several of the Figures from both Applicants' publication as well as Sutton, to illustrate how the structure of these instruments differ.

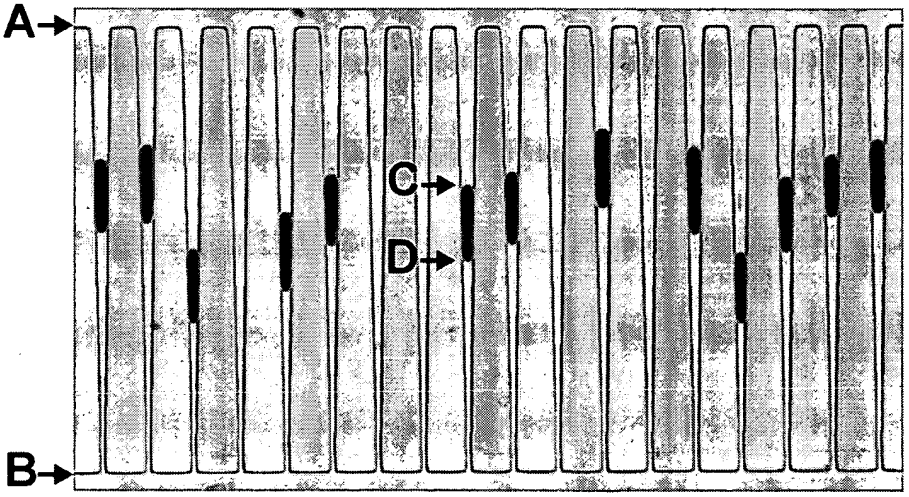
The present invention teaches several different embodiments of the instrument. One embodiment provides a series of channels of different shapes and sizes, for example as illustrated in Figure 1 of Gifford et al.:



The channels of the instrument can be wedge-shaped, as depicted in Figure 3 of Gifford:

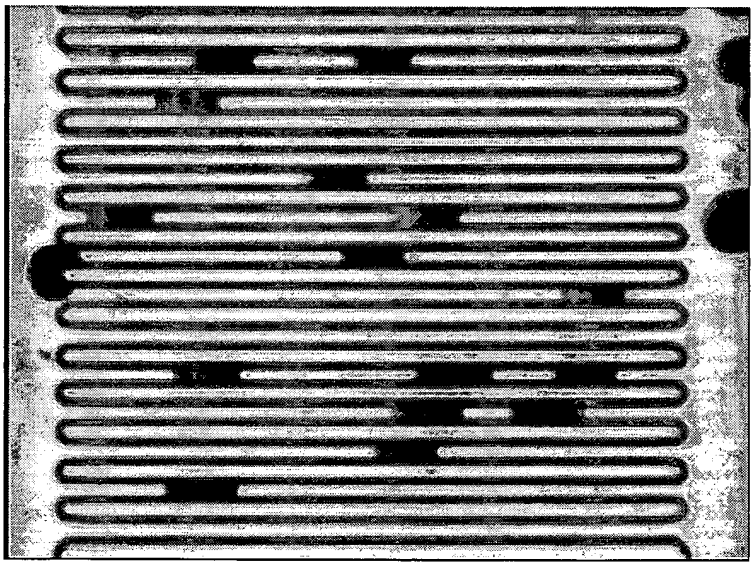


As depicted in Figure 5 of Gifford, shown below, these wedge-shaped channels function to arrest red cells as they transit the channel. Cells enter by the wider side (A) and are trapped as the microchannel narrows going toward exit (B). The measurements of the top (C) and the bottom (D) of each cell which has been arrested in a channel are used to calculate the cell's area and volume.

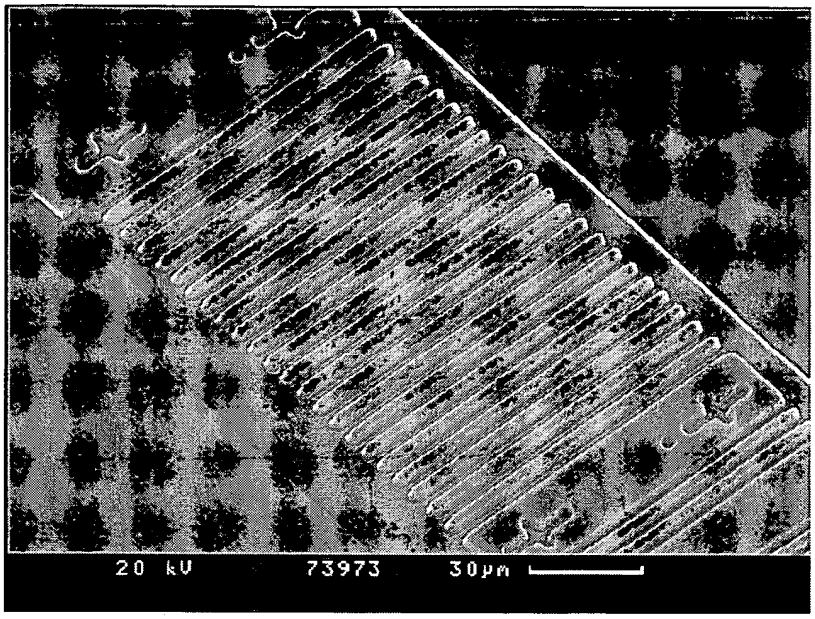


In contrast, the instrument of Sutton is designed to measure the flow of red cells as they transit through the instrument. The channels are not shaped, for example, as above from wider to narrower, to trap the cell. Consequently, cells which are too large will not enter or traverse the microchannel. Thus, the Sutton microarray is necessarily limited to measuring the transit of cells through the microchannels, not to capture cells. The structure of the array differs from that of claim 1.

This fundamental difference in the structure of the Sutton instrument is reflected in the function which allows multiple red cells to flow through a single channel, as depicted in Figure 5 of Sutton, reproduced below:



Furthermore, the Sutton array does not comprise multiple rows of channels having differing cross-sectional areas, as depicted for example in Figure 1 of Gifford, above, but instead has only a single row of channels. This is clearly seen in Figure 1 of Sutton:



Thus, it is abundantly clear that the instrument of the present invention and the Sutton instrument have fundamental structural differences which are designed to accomplish their different functions.

The Examiner has contended that the present invention is not structurally different from the Sutton instrument based on her interpretation of the claims. Applicants respectfully disagree. For example, the structure is wedge-shaped with a wider entry end than exit end, in another embodiment the structure has multiple rows with the entry row having a wider cross-sectional area than a later row. This structure is designed to meet the requirement of the claim that the cell does not leave the microchannel but is constrained to remain in the microchannel.

The Examiner has also contended that the gradient array of claim 2 is anticipated by Sutton, which teaches an array with groups of channels of different widths. Applicants respectfully submit that the Examiner is overlooking a requirement of the array of claim 2, namely that the microchannels are arranged in rows in such a manner that it forms a gradient for capturing a cell. Applicants have amended claim 2 to expedite prosecution by making explicit that which was implicit, namely that the gradient array has at least two rows of microchannels. The present invention provides many variations of sequential channels. Nothing in Sutton teaches or suggests using sequential rows of increasingly smaller microchannels to capture cells. Applicants respectfully submit that this amendment has obviated the rejection.

The Examiner has also taken the position that Sutton teaches the use of "substantially wedge-shaped" channels as recited in claim 4. To support this contention, the Examiner points to a single sentence in the Discussion section of Sutton which refers to the theoretical construction of channels with "stepped widths." Applicants respectfully submit that the meaning of "stepped widths" is not obviously synonymous with a wedge-shaped channel. Applicants further submit that the mere description of such a channel in no way teaches the present invention, for the following reasons. Sutton provides no actual description of such an instrument. Sutton is merely discussing design possibilities enabled by advances in techniques for channel microfabrication, and in no way describes an instrument with wedge-shaped channels of the instant invention. Significantly, everything in Sutton **teaches directly away** from the present instrument, because it describes a method which **relies** on the **transit** of a cell through the channel; if a cell gets stuck in the Sutton instrument, it would be impossible to use its method to calculate its flow velocity. Accordingly, applicants respectfully submit that nothing in Sutton teaches the use of wedge-shaped channels to capture cells.

Accordingly, applicants respectfully submit that these rejections of the claims should be withdrawn.

Claims 1 – 18 were rejected under 35 U.S.C. § 102(b) as being anticipated by Brody.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

Like Sutton, Brody is directed to the real-time analysis of red blood cells during their transit through microchannels. The title and abstract clearly indicate that Brody looks at cells "flowing through the bed at physiological speeds" (Abstract). Like Sutton, Brody uses video microscopy to track the movement of single cells through the array. Figures 2, 5, 8, and 9 of Brody all show images of cells moving through an array. Thus, the structure of the Brody array is designed to accomplish its function, which is again entirely dependent upon the continued flow of the cells through the microchannels. In contrast, claim 1 of the present invention creates a structure for an entirely different function, to capture the cell, blocking its further movement through the array.

In issuing this rejection, the Examiner has essentially repeated the arguments made in rejecting the claims over Sutton, namely, that the design of the Brody instrument is the same as the design of the instant instrument. Applicants respectfully submit that for all of the reasons outlined above with respect to Sutton, including all of the amendments to the claims, Brody does not anticipate the claims of the present invention. For example, Brody does not teach wedge-shaped channels, wider at the entrance than exit. Similarly, the Brody array does not teach a configuration of a gradient of microchannels of decreasing width, designed to capture the red blood cell and block its further movement through the array. Accordingly, applicants respectfully submit that these rejections of the claims should be withdrawn.

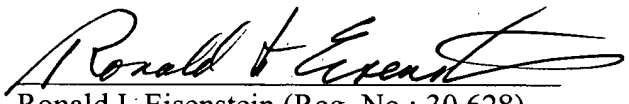
Accordingly, in view of the foregoing, applicants respectfully submit that all claims comply with 35 U.S.C. § 102(b).

In view of the foregoing, applicants submit that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our Deposit Account No. 50-0850.

Respectfully submitted,

Date: August 1, 2005



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